Citation:

Toledo E, Delgado-Rodríguez M, Estruch R, Salas-Salvadó J, Corella D, Gomez-Gracia E, Fiol M, Lamuela-Raventós RM, Schröder H, Arós F, Ros E, Ruíz-Gutiérrez V, Lapetra J, Conde-Herrera M, Sáez G, Vinyoles E, Martínez-González MA. Low-fat dairy products and blood pressure: Follow-up of 2,290 older persons at high cardiovascular risk participating in the PREDIMED study. *Br J Nutr.* 2009 Jan; 101 (1): 59-67. Epub 2008 May 20.

PubMed ID: 18492300

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To assess the relationship between low-fat dairy product intake and blood pressure (BP) levels and their changes after 12-month follow-up in a cohort of asymptomatic older persons at high cardiovascular risk recruited into a large-scale trial assessing the effects of Mediterranean diets on cardiovascular outcomes.

Inclusion Criteria:

- Men age 55 to 80 years and women age 60 to 80 years
- No previously documented cardiovascular disease (CVD), but at high cardiovascular risk
- Either type 2 diabetes (T2D) or at least three of the following risk factors:
    - Current smoking
    - Hypertension (HTN)
    - Gyperlipidemia
    - Low HDL-cholesterol
    - Overweight/obesity
    - Family history of premature coronary heart disease (CHD).

Exclusion Criteria:

- Participants with missing questionnaire or BP data
- Participants reporting extreme total energy intakes.

Description of Study Protocol:

Recruitment

Participants from the PREDIMED trial.

Design

- The intervention of the PREDIMED trial (parallel-group, randomized controlled clinical trial) did not include intake of low-fat dairy products as part of the intervention; thus, in the present analysis, data from this trial were analyzed as an observational cohort study
- Cross-sectional analyses in a cohort of 2,290 participants was conducted at baseline and at the end of follow-up; additionally, longitudinal analyses over 12-months were completed.

Dietary Intake/Dietary Assessment Methodology

Validated semi-quantitative food-frequency questionnaire (FFQ) (137-item); dairy products assessed in 15 items.

Blinding Used

Not applicable.

Intervention

Not applicable. (The PREDIMED trial assessed three diets: Low-fat; Mediterranean supplemented with nuts; Mediterranean supplemented with olive oil. However, for this article, all participants were analyzed together in an observational cohort study).

Statistical Analysis

- Participants were divided into five groups according to quintiles of consumption of low-fat dairy or whole-fat dairy products
- First, the crude means for systolic and diastolic blood pressure (SBP and DBP) were compared across quintiles of dairy product consumption (separately for low-fat and whole-fat items)
- Afterwards, multivariable linear regression models were fit to control for potential confounders
- Multivariable linear regression models were fitted considering current BMI as a potential confounder. However, current BMI may also be considered as an intermediate variable in the association between low-fat dairy consumption and BP and, therefore, the authors constructed models both adjusted for BMI and not adjusted for BMI
- For each exposure (low-fat and whole-fat dairy products) five multivariable linear regression models were fitted:
    - A baseline cross-sectional analysis (exposure: Baseline dairy product consumption; outcome: baseline BP)
    - A 12-month cross-sectional analysis (exposure: Dairy product consumption after 12 months; outcome: BP after 12 months)
    - A conventional longitudinal analysis (exposure: Baseline dairy product consumption; outcome: BP after 12 months)
    - A longitudinal analysis with BP changes as outcome (exposure: Baseline dairy product consumption; outcome: BP changes during follow-up)
    - A dynamic longitudinal analysis (exposure: Changes in dairy product consumption; outcome: Changes in BP).
- For linear trend tests, each quintile of dairy consumption was assigned its median value and the resulting variable was considered as quantitative in the multivariable analyses.

Confidence intervals at 95% were calculated in every model including all the data.

Data Collection Summary:

Timing of Measurements

Baseline and 12-month follow-up.

Dependent Variables

Blood pressure (measured by trained personnel).

Independent Variables

- Low-fat dairy product intake (including partially skimmed milk, skimmed milk, skimmed yogurt and cottage cheese)
- Whole-fat dairy product intake.

Control Variables

- Smoking
- Education level
- Physical activity, BMI
- Treatment with non-steroid inflammatory drugs, treatment with angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists, treatment with other antihypertensive drugs
- Hyperlipidemia
- T2D
- Total energy intake
- Intake of alcohol and sodium
- Treatment with drugs that may increase calcaemia
- Treatment with drugs that may decrease calcaemia
- Treatment with potassium (K) supplements
- Dietary intake of K, Calcium, Magnesium and protein from sources other than low-fat dairy products
- Saturated fatty acids, MUFA, fiber, fruit and vegetables.

Description of Actual Data Sample:

- *Initial N*: 2,392
- *Attrition (final N):* 2,290
- *Mean age:* Approximately 67 years (SD: Approximately six years)
    - Men: 55-80 years
    - Women: 60-80 years
- *Ethnicity:* Not mentioned, likely to be mostly European
- *Other relevant demographics:* None
- *Anthropometrics:* Body Mass Index (BMI) (SD) by quartiles of low-fat dairy consumption:
    - Q1: 29.6 (3.5) kg/m^2
    - Q2: 29.5 (3.5) kg/m^2
    - Q3: 29.9 (3.6) kg/m^2
    - Q4: 29.7 (3.7) kg/m^2

- Q5: 30.0 (4.3) kg/m^2
- *Location:* Spain.

Summary of Results:

Key Findings

- A statistically significant inverse association between low-fat dairy product intake and SBP was observed for the 12-month longitudinal analysis
- In the longitudinal analysis, the adjusted SBP and DBP were significantly lower in the highest quintile of low-fat dairy product intake (-4.2 (95% CI: -6.9, -1.4) and -1.8 (95% CI: -3.2, -0.4) mmHg respectively), whereas the point estimates for the difference in DBP indicated a modest non-significant inverse association
- No significant trends were observed in the analyses using whole-fat dairy product consumption as exposure.

Author Conclusion:

Intake of low-fat dairy products was inversely associated with BP in an older population at high cardiovascular risk, suggesting a possible protective effect against HTN.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes

1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A

4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes

7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes